Remarks

This application has been carefully reviewed in light of the Office Action mailed May 4, 2005. Claims 1-34 are pending and stand rejected. Reconsideration and allowance of Claims 1-34 is respectfully requested in view of the following remarks.

Rejections Under 35 U.S.C. § 103

The Office Action rejects Claims 1-34 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 6,216,540 to Nelson, et al. ("*Nelson*"). Applicants respectfully traverse. As an initial matter, Applicants refer the Examiner to the analogy provided at pages 7-9 of Applicants' Response dated November 4, 2004, a review of which may further prosecution.

Claim 1 recites

> a method, comprising:
>
> introducing an exogenous fluorescent contrast agent into a biologic tissue, the tissue multiply scattering light with a mean time-of-flight, and the agent having a fluorescence lifetime within a factor of about ten of the mean time-of- flight;
>
> exposing the tissue to an excitation light with a predetermined time-varying intensity;
>
> detecting a light emission from the tissue in response to said exposing;
>
> generating an image of the tissue by mapping spatial variation of a level of a fluorescence characteristic of the tissue from the light emission in accordance with a mathematical expression modeling multiple light scattering behavior of the tissue; and
>
> wherein the agent is selected in accordance with a predetermined relationship between degree of image contrast and at least one of fluorescence yield or the fluorescence lifetime.

The rejection of Claim 1 is improper at least because *Nelson* fails to disclose many of the limitations of this claim. For example, *Nelson* fails to disclose introducing an exogenous fluorescent contrast agent into a biologic tissue. Nowhere in *Nelson* can there be found a teaching of introducing an exogenous fluorescent contrast agent into a biologic tissue. The

Office Action asserts, "Nelson et al discloses a method comprising introducing an exogenous fluorescent contrast agent into a biological tissue," but fails to identify any portion of *Nelson* that teaches this limitation. The only portion of *Nelson* cited in rejecting Claim 1 is col. 19, Lines 22-53; Col. 24, Line 56 - Col. 25, Line 43; Col. 26, Lines 5-32, but the Office Action does not identify whether it contends these portions of *Nelson* disclose introducing an exogenous fluorescent contrast agent into a biologic tissue or what elements in these portions it contends meets this limitation. Applicants have carefully reviewed these portions of *Nelson* as well as the remaining portions of *Nelson* and can find no teaching of introducing an exogenous fluorescent contrast agent into a biologic tissue.

Column 25, line 35 of *Nelson* mentions fluorescence, but there is no disclosure of introducing an exogenous fluorescent contrast agent. To the extent any more information may be gleamed from the relatively sparse disclosure of *Nelson* regarding fluorescence, that information would suggest that the object being imagined is a radiator of fluorescence radiation, not that an exogenous fluorescent contrast agent is introduced into a biological tissue. Because tissues have fluorescence in the UV wavelength range, this passage suggests, if anything, that endogenous (i.e. native to the tissue) fluorescence is being measured.

Further, no portion of the cited reference relied on in the Office Action even mentions a contrast agent. Applicants have carefully reviewed the cited reference and did find mention of a contrast agent at Col. 12, lines 12-49 (portions not referenced to in the Office Action), and confirmed that *Nelson* fails to disclose use of a fluorescent contrast agent, as claimed. Although listing several types of contrast agents, a fluorescent contrast agent is not disclosed. For a least this reason, Claim 1 is allowable.

Claim 1 is allowable also because the cited reference does not disclose "the agent having a fluorescence lifetime within a factor of about ten of the mean time-of-flight." Indeed, the cited reference provides no teaching regarding the appropriate fluorescence lifetime of the agent. In rejecting Claim 1, the Office Action states:

> The degree of fluorescence and its lifetime characteristics is dependent on the absorption characteristics of the contrast agent and specificity of the tissue or organs targeted. Therefore, the lifetime factor of the fluorescence is a design choice limited by the radiation absorption and how fast the body circulates the materials out the physiological system. Therefore, it would have been obvious to one having an ordinary skill in the art at the time the invention was made to vary the fluorescence lifetime to the specificity of the contrast application with varying degree of radiation absorption due to tissue characteristics as well as radiation

intensity variation with the teachings of *Nelson* et al to achieve the claimed invention.

But fluorescence lifetime does not refer to the circulation time in the body, but rather a photophysical property of the fluorescent contrast agent. Thus, it would not be obvious to modify the cited reference as suggested in the Office Action. For at least this additional reason, Claim 1 is allowable.

Claim 1 is also allowable because the cited reference does not teach "exposing the tissue to an excitation light" and "detecting a light emission from the tissue in response." As described in Applicants' specification, the excitation light excites the contrast agent at the excitation wavelength of the contrast agent, causing emission of light in response at an emission wavelength. There is no teaching in the cited reference of such use of "excitation light" and detection of "light emission" in response. For at least this additional reason, Claim 1 is allowable.

Claim 1 is also allowable because the cited reference fails to disclose the agent is selected in accordance with a predetermined relationship between degree of image contrast and at least one of fluorescence yield or the fluorescence lifetime. As described above, the Office Action relies on the flawed premise that fluorescence lifetime relates to circulation time in the body, as opposed to a photophysical property of a fluorescent contrast agent in stating that varying the fluorescence lifetime is an obvious design choice. As relying on a flawed premise, the conclusion of obviousness is also flawed. There is simply no teaching in the cited reference or motivation in the art to modify the reference to provide that the agent is selected in accordance with a predetermined relationship between degree of image contrast and at least one of fluorescence yield or the fluorescence lifetime. For at least this additional reason, Claim 1 is allowable.

For the above reasons, Claim 1 is allowable, as are the claims depending therefrom. Independent Claims 11, 17 and 23 are allowable for analogous reasons. Applicants respectfully request consideration and favorable action.

Conclusion

Applicants have now made an earnest attempt to place this case in condition for immediate allowance. For the foregoing reasons and for other apparent reasons, Applicants respectfully request allowance of all pending claims.

If the Examiner feels that prosecution of the present Application may be advanced in any way by a telephone conference, the Examiner is invited to contact the undersigned attorney at 214-953-6447.

Applicants do not believe that any fees are due. However, the Commissioner is hereby authorized to charge any fees or credit any overpayments to Deposit Account No. 02-0384 of Baker Botts L.L.P.

Respectfully submitted,

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